A Literature Review of the Association Between the Mediterranean Diet and Cancer: The Tale of Two Regions

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Abstract

According to the World Health Organization (WHO), cancer is the second leading cause of death worldwide after cardiovascular disease. Among women and men, breast and prostate cancers are respectively the most commonly diagnosed and the leading causes of death (WHO, 2017). Much research has been conducted in an attempt to determine the risk factors affecting the initiation, promotion, and proliferation of tumor cells. Obesity has been identified as one such modifiable risk factor. Evidence from studies investigating the relationship between body-mass index (BMI) and the risk for developing 22 different types of cancer shows that a higher BMI is associated with a greater risk of cancer diagnosis (Bhaskaran et al., 2014). Obesity is highly prevalent in the United States and also continues to rise globally. However, in Europe, particularly in the Mediterranean region, the obesity rates are lower than that of the United States. In addition, cancer incidence and mortality rates are lower in these regions. Thus, attention is drawn towards the differences in dietary lifestyle between the United States and the Mediterranean regions. This literature review described and compared cancer disease outcomes among populations consuming the Mediterranean diet against those populations consuming the Westernized diet. Studies were identified using the search engines PubMed, EBSCOhost, and WorldCat@OSU, and the topics focused on were on the Mediterranean and Westernized dietary patterns in relation to cancer development, outcome, and mortality. Evidence from this literature review shows that individual adherence to a Mediterranean diet both in the Mediterranean region and the United States was associated with a decreased cancer risk and mortality. The adoption of the Mediterranean diet as part of a healthy lifestyle needs to be encouraged among Americans as part of an intervention for reducing cancer risk and/or improving disease outcomes.

Chapter 1: Introduction

In the United States and globally, cancer is the second leading cause of death after cardiovascular disease (WHO, 2017). Across all ethnicities and races in the United States, breast, lung, and colorectal cancers are the most commonly diagnosed among women, and prostate, lung, and colorectal cancers are the most commonly diagnosed among men (CDC, 2016). In addition, these cancers are also the leading cases of cancer death for both genders (WHO, 2017). Much research has been done on the different lifestyle, environmental, and genetic factors that could influence the initiation and promotion of cancer tumors in the body. One such lifestyle factor that has been studied is obesity. An investigation of the relationship between body mass index and the risk for developing 22 different types of cancer found a higher body mass index (BMI) to be associated with an increased risk for developing cancer (Bhaskaran et al., 2014). Furthermore, obesity is not only associated with an increased risk for cancer development, but also for cancer progression. In a study looking at the association of obesity and prostate cancer metastasis and mortality, it was found that obesity was associated with an increased risk for these two outcomes (Gong, Agalliu, Lin, Stanford, & Kristal, 2007).

Obesity is highly prevalent in the United States and continues to be a public health challenge. A 2002 study of the U.S. population using the National Health and Nutrition Examination Survey (NHANES) data, found that 65.1% of American adults were overweight or obese, with 30.4% being obese and 4.9% extremely obese (Hedley et al., 2004). A recent study using newer NHANES data reports obesity rates among gender as follows: 35% of men and 40.4% of women are obese, while 5.5% of men and 9.9% of women are in stage III obesity. In addition, the statistics from both sexes amounted to 37.7% overall obesity with 7.7% having obesity stage III (Flegal, Kruszon-Moran, Carroll, Eryar, & Ogden, 2016).

Similar to trends observed in the U.S., obesity continues to rise globally. Nevertheless in Europe, particularly in the Mediterranean regions, the rates are not as quickly growing and high compared to the United States (Chan, 2017). The World Health Organization (WHO) in the European Region roughly estimates that around 23% of women and 20% of men are obese, but overall, between 10 and 30 percent of adults are obese (WHO/Europe, 2017). More specifically, the prevalence of obesity in men from Western Europe (including the Mediterranean region) was 20% and the prevalence in women was between 15% and 20% (Chan, 2017). A study by Gallus et al. (2015) looked at the obesity prevalence among individual European countries and found that the lowest prevalence of obesity was in the Mediterranean region. Specifically, obesity statistics in the Mediterranean countries were, at the highest, 14% in Spain and, at the lowest, 7.6% in Italy (Gallus et al., 2015). Thus, the overall prevalence of obesity in Europe and specifically in the Mediterranean region is much lower than the obesity prevalence found in the United States.

With such marked differences in obesity prevalence between these two regions, a critical look at the differences in diet and lifestyles and the impact on obesity prevalence is warranted. Attention has been drawn to the Westernized diet, characterized by a high consumption of red meat, processed foods, refined carbohydrates, and low consumption of fruits, vegetables, quality fats, and complex carbohydrates, and its link to an increased risk of developing chronic diseases. In contrast, researchers and health professionals alike have turned to the Mediterranean diet, as defined by an increased consumption of olive oil, fish, complex carbohydrates such as legumes and whole grains, fruits, and vegetables, and its role in the prevention of such chronic diseases associated with the consumption of a Westernized diet.

The goal of this literature review is to describe and compare cancer disease outcomes, among populations consuming the Mediterranean diet to those populations consuming the Westernized diet.

Chapter 2: Background

The Mediterranean Diet versus the Westernized Diet

The Mediterranean diet has its origins from the Arabs and Phoenicians, and each country in the region today has unique adaptations to the diet. There are, however, core foods within the Mediterranean diet that remain standard in each country. These are whole grains, legumes, nuts, fruits, vegetables, olive oil, and fish, with a moderate intake of red wine and little to no intake of red meat and processed foods (Heltostky, 2009). In contrast to the high consumption of processed foods observed in the Westernized diet, Slimani and colleagues (2009) showed that the consumption of processed foods in Western Europe is low and consists only of foods such as pasta, rice, milk, and bread. To the contrary, the Western diet pattern followed in the United States consists of a high consumption of meat, specifically red meat, dairy products, processed foods, simple carbohydrates, and low to moderate intakes of fruits and vegetables. Other definitions of the Western dietary food pattern have included consumption of high-fat dairy foods, gravy and sauces, fast foods, potatoes, margarine, and high-fat and high-sugar desserts (Murtaugh et al., 2008).

In addition to the specific food groups highlighted as part of the Mediterranean diet and Western diet, each dietary pattern also follows a drastically different lifestyle and approach to food. It has been argued that the increase in access to processed and "fast" foods has led Americans to develop an increasingly sedentary lifestyle compared to other populations in the developed world and also to the Nomadic tribes previously settled in these territories. It is theorized that around 10,000 years ago, there was a movement from hunter-gatherers to that of agriculturalists, including the domestication of animals. With this movement, the notion of a sedentary lifestyle began since it was no longer necessary to hunt for every meal. As time progressed, innovative technology, such as farming machinery and mechanized milling tools for

grains that made them more refined, was invented, which made the adoption of this new lifestyle much easier (Heltostky, 2009). In fact, around 85.3% of cereals consumed in an American diet are highly processed refined grains (Cordain et al., 2005). Many argue that the Industrial Revolution brought about this change in consumption patterns of the foods that define the Western diet, namely refined carbohydrates, red meat, sugar, and processed foods, since the access and availability of these foods became widespread throughout the nation (Helstosky, 2009).

The Mediterranean diet was introduced to the Mediterranean region through trade with the Arabs and Phoenicians. However, foods such as bread, fish, vegetables, olive oil, and drink such as wine were adapted from the ancient Roman and Greek culture and integrated into the Mediterranean cuisine (Helstosky, 2009). Over time, the Mediterranean food culture and way of life has been passed down from generation to generation and has even been adopted in many parts of the world.

The Science Behind the Food

Studies on the Mediterranean diet have examined its ability in lowering risks for developing diseases such as cardiovascular disease, diabetes, cancer, and other obesity related diseases. Much attention has been focused on food properties (e.g. phytochemicals found in plant-based foods) that may contribute to these benefits. Another focus of research has been the sources of animal protein as a potential for disease risk. The Mediterranean diet promotes the consumption of fish over red meat unlike the Westernized diet. Pellatt, Slattery, Mullany, Wolff, and Pellatt (2016) investigated dietary intake and the influence of gene expression on disease prevalence. The study demonstrated that red meat activates pro-carcinogenic genes, making it easy to become susceptible to developing cancer later on in life. Thus, it was concluded that red

meat consumption, particularly high-fat red meat consumption, is associated with an increased risk of multiple chronic diseases, especially cancer (Pellatt et al., 2016).

Similarly, the Westernized diet also promotes the consumption of more omega-6 fatty acid rich foods—such as refined vegetable oils, which are utilized mostly in processed foods—compared to omega-3 fatty acids. This imbalance in the omega-6 to omega-3 ratio could possibly contribute to increased inflammatory markers in the body and potentially contribute to tumor formation and cancer growth (Simopoulos, 2002). Compared to omega-6 fatty acids, the main source of omega-3 fatty acids is found in both animal and plant sources, but the eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) found in marine sources are associated with a decreased risk for chronic diseases including cancer and inflammation. A study by Liang et al. (2016) investigated the effects of omega-3 fatty acids and omega-6 fatty acids on prostate tumor growth in vitro. Mice were either fed a diet comprising of 30% total calories from omega-6s from corn oil or omega-3s from menhaden oil, while also maintaining the same caloric consumption in both groups. The mice were then injected with cells that promoted tumor growth and then randomized into either the omega-6 fed group or the omega-3 fed group. The mice were later sacrificed to assess the outcomes on tumor growth by looking at the different inflammatory responses, namely macrophages, interleukins, and cytokines. Results showed that the mice fed the omega-3 rich diet had significantly decreased growth rate of the tumor. In addition, there were lower inflammatory markers present in the tumors from the omega-3 mice group, suggesting that omega-3 fatty acids may have a role in altering gene expression. Tumor cells operate by creating an inflammatory response that then initiates an immunity response in the body, which increases the presence of macrophages, interleukins, and cytokines. Though this is the body's natural immunity response, these inflammatory markers are associated with

promoting the growth of the tumor. Therefore, with the decreased gene expression of these inflammatory responses by omega-3 fatty acids, decreases in tumor growth occurred (Liang et al., 2016).

Findings from studies in mice models have been confirmed by investigations in humans. In a prospective cohort study, Leitzmann et al. (2004) compared the effect of dietary intake of omega-3 fatty acids—specifically alpha-linolenic acid (ALA) from meat/dairy sources and non-animal sources versus DHA and EPA and omega-6 fatty acids—on the risk for the development of prostate cancer. Results showed that higher consumption of EPA and DHA was associated with a reduced risk in development of prostate cancer. The study also investigated the effect of consuming these essential fatty acids from supplements. The effects were found to be weaker for supplement consumption compared to dietary consumption, which suggests a need for dietary consumption of EPA and DHA to observe these benefits (Leitzmann et al., 2004). Similar effects of omega-3 fatty acid consumption were seen as related to breast cancer risk. In a study by Kim et al. (2009), researchers observed the association between fatty fish consumption and overall breast cancer risk. Results indicated that in both pre- and post-menopausal women, a higher consumption of fatty fish rich in omega-3 fatty acids was associated with a decreased risk in development of breast cancer.

Other health benefits of the Mediterranean diet come from the increased intake in fruits and vegetables, which are highly concentrated in a variety of phytochemicals. The American Institute for Cancer Research (2015) provides a set of evidence-based guidelines for different aspects of diet and lifestyle that aid with cancer prevention and survivorship. These guidelines promote the consumption of fruits and vegetables because of their phytochemical content. Phytochemicals are found in plants and are described as “biologically active compounds” that

behave as antioxidants, which can prevent cell proliferation that leads to cancer development. Phytochemicals are not essential in the diet, but there is evidence to support their promotion of many beneficial health outcomes (World Cancer Research Fund, 2007).

Cancer Incidence and Mortality

Cancer is now the second leading cause of death worldwide, with the highest cancer incidence among men and women being prostate cancer and breast cancer, respectively (WHO, 2017). According to the American Cancer Society, the three highest cancer incidences for both sexes are lung/bronchus, colon/rectum, and breast cancer (women) and prostate cancer (men). In addition, these cancers were found to be the leading cause of mortality for both sexes, with the highest mortality rates being among those diagnosed with lung and bronchus cancer and then prostate cancer for males and breast cancer for females (American Cancer Society, 2015). Similar rates were found in Europe: the incidence of breast and prostate cancer is reported to be the highest in the respective genders, followed by lung and colorectal cancers (WHO, 2014). However, according to WHO, incidence of breast cancer is lower in Southern Europe as well as Central/Eastern Europe, which are located in the Mediterranean region, compared to the United States. With regard to prostate cancer, autopsy studies report the highest prevalence rates among individuals of American descent, while lower prevalence was found among men of Mediterranean descent (Haas, Delongchamps, Brawley, Wang, & de la Roza, 2008). In addition to lower incidence, the Mediterranean regions also have lower mortality rates than North America. A 5-year all-cancer mortality prevalence data, excluding non-melanoma skin cancer, for both sexes was found to be lower for Eastern Mediterranean regions and the European region in general compared to the United States (WHO, 2012). Though evidence suggests lower incidence of cancer in the Mediterranean regions compared to the United States, it must be noted

that a possible reason for higher incidence statistics in the United States is due to early testing and detection of tumors, e.g. prostate specific antigen (PSA) testing for males (WHO, 2012).

Chapter 3: Methods

This literature review is a comparative review that showcases the differences between the Mediterranean diet and the Westernized diet and their effects on cancer. There were no set limitations on publication years; however, the article search comprised of articles published between the years 1995 and 2016. The three databases that were used to search for peer-reviewed literature articles were PubMed, EBSCOhost, and WorldCat@OSU. The combined search terms used were "Mediterranean diet," "Westernized diet," "cancer," "prostate cancer," "breast cancer," "cancer incidence," and "cancer prevalence." Though there were no limitations on types of research articles used, prospective cohort studies were mainly utilized. In addition, in order to define and establish the foods and lifestyle of the Mediterranean diet, an additional book resource was studied and used on such topic.

Chapter 4: Results and Discussion

The Westernized and Mediterranean Diets Effect on Cancer: the United States

With high incidence and prevalence of not only cancer, but also other chronic diseases such as cardiovascular disease and diabetes, increasing attention has been turned to the effects of modifiable risk factors such as diet and lifestyle on the development of these chronic diseases. Several observational studies in the United States have investigated the health effects of the Westernized dietary pattern on cancer development risk and prognosis. Schleper et al. (2016) studied the effects of a Westernized diet—characterized by high consumption of red meat, high consumption of dairy, and a low consumption of cruciferous vegetables—on body mass index (BMI) and the effects on prostate cancer prognosis and development. Their findings showed that a higher BMI due to adherence to the Westernized dietary patterns corresponded to an increased risk in both prostate cancer development and aggressiveness during diagnosis. It was therefore suggested that men, particularly those with higher BMIs, receive diet education to improve weight status, and, subsequently, prostate cancer incidence and prognosis (Schleper et al., 2016).

Another prospective cohort study of participants in the Physicians' Health Study investigated the effects of two different dietary patterns: the Prudent pattern (similar to the Mediterranean dietary pattern) and the Western pattern on prostate cancer mortality. The Prudent pattern was defined as higher intakes of vegetables, fruits, whole grains, legumes, fish, olive oil, and soy products, while the Western pattern was defined as higher intakes of red and processed meats, potatoes, high-fat dairy products, refined grains, sweets/desserts, and snacks. Findings showed the Western diet to be associated with a higher mortality rate for prostate cancer; greater adherence was associated with a 67% increased risk of overall mortality. In contrast, those that

followed the Prudent diet had a 36% reduced risk of overall mortality due to prostate cancer (Yang et al., 2015).

In the Four-Corners Breast Cancer Study, researchers studied the effects of five different dietary patterns—Western, Prudent, Native Mexican, Mediterranean, and Dieter—on breast cancer risk in Hispanic and non-Hispanic women. As stated earlier, the Prudent diet is similar to the Mediterranean dietary pattern, with the difference being the addition of soy products. The Native Mexican diet contained a higher consumption of typical Mexican cuisine, such as Mexican cheeses, soups, meat dishes, legumes, and tomato-based sauces. The Dieter pattern was defined as the consumption of diet beverages and sugar substitutes and low-fat dairy, margarine, and desserts and as avoidance of high-fat dairy products, soda beverages, and butter. Results indicated that the dietary patterns of the Western diet were associated with a greater risk for breast cancer development. In contrast, it was found that intake adherent to the Mediterranean diet was found to be associated with reduced risk for breast cancer development (Murtaugh et al., 2008). Similarly, a prospective study from the National Institute of Heath-American Association of Retired Persons (NIH-AARP) Diet and Health Cohort Study examined the effects of a Mediterranean dietary pattern on cancer mortality. Results showed an association between a greater adherence to the Mediterranean dietary patterns and a reduction in all-cause mortality in both males and females diagnosed with both cancer and cardiovascular disease. The authors postulated that a possible explanation for this decreased risk was the protective effects of the Mediterranean dietary pattern in lowering chronic inflammation. This is because lower levels of traditional inflammatory markers (C-reactive protein, interleukins, homocysteine) were observed in individuals adhering to the Mediterranean diet. Since chronic inflammation has been

associated with a possible higher risk of developing cancer, the decrease in these markers due to the Mediterranean diet may help decrease cancer risk (Mitrou et al., 2007).

The Westernized and Mediterranean Diets Effect on Cancer: the Mediterranean Region

In order to quantitatively assess adherence to the Mediterranean dietary pattern, researchers have developed different scales to measure adherence. One such scale was developed by Trichopoulou et al. (1995) in a study assessing the effects of a Mediterranean diet on survival rates in an elderly Greek population. This 9-point based scale system is dependent upon different dietary factors typical to a Mediterranean diet, such as high consumption of fruits, vegetables, fish, cereals, and monounsaturated fats (olive oil) compared to saturated fats, a moderate consumption of alcohol and milk/dairy products, and a low consumption of meat and meat products. This point system is used in many research studies today, particularly in a large prospective cohort study in Europe.

When observations about the Mediterranean diet on chronic disease outcomes and prevention first began, the World Health Organization began a prospective cohort study named the European Prospective Investigation into Cancer and Nutrition (EPIC) that has been following inhabitants from 10 different Western European countries. The overall objective of the study was to "investigate the relationships between diet, nutritional status, lifestyle and environmental factors, and the incidence of cancer and other chronic diseases" (WHO, 2016). The EPIC study is currently one of the largest cohort studies in the world and many other studies have emerged from it. One such sub study investigated the overall consumption of processed foods to the diet in European countries. The results indicate that in Mediterranean countries such as Greece, Spain, Italy, and France (classified as Southern Europe), the overall contribution of processed foods to the diet was much lower compared to the other countries investigated, such as Germany,

the United Kingdom, and the Netherlands (classified as Northern Europe). Inhabitants in these latter countries consumed a diet similar to a Westernized diet, especially with the respect to the consumption of processed foods (Slimani et al., 2009).

The EPIC cohort study observed the adherence to a Mediterranean dietary pattern on the effects of cancer risk. Participants were included from several European countries, varying from those in the Mediterranean region and those in the Northern European region where a Westernized diet is more commonly consumed. Results indicate that a greater adherence to Mediterranean dietary patterns was associated with decreased cancer risk, and these results applied to both participants from Mediterranean countries and participants from non-Mediterranean countries (Couto et al., 2011).

A study observing the effects of a higher Mediterranean diet consumption and cancer incidence in the Greek EPIC cohort study also found that greater adherence to the Mediterranean diet coincided with a lower overall cancer incidence. Another finding was that either reducing meat intake and increasing consumption of legumes or increasing vegetable intake and substituting olive oil for saturated fats (specifically butter) was associated with a 12% reduction in overall cancer incidence (Benetou et al., 2008).

Another study from the EPIC prospective cohort study looked at the associations of the Western and Mediterranean dietary patterns on the risk for breast cancer development in postmenopausal women living in France. Dietary data was obtained based on questionnaires and information on breast cancer occurrence was also obtained. Results showed a positive association between a dietary pattern adhering closely to a Westernized diet and increased breast cancer risk. Conversely, an inverse association between adherence to a Mediterranean dietary pattern and breast cancer risk was observed (Cottet et al., 2009). Furthermore, a case-control

study explored the protective benefits of the Mediterranean diet in women diagnosed with breast cancer and women matched in age but without breast cancer. Results showed that there is an inverse relationship between breast cancer risk and adherence to a Mediterranean diet. In fact, it was found that the foods that had a greater contribution to lowering the risk for breast cancer were non-refined cereals, vegetables, fruits, and a moderate consumption of alcohol; conversely, foods that may contribute to breast cancer were red meat and meat products (Mourouti et al., 2014).

Prostate cancer has grown globally over the years, especially among men in European countries. However, it has been found that those following a Mediterranean diet—specifically in southern Europe—have lower prostate cancer incidence and mortality rates (Bray et al., 2010). In a review by López-Guarnido et al. (2015), researchers noted that countries adhering to a more traditional Mediterranean diet, in particular countries in Southern Europe, have both a lower prostate cancer incidence and mortality. One important finding from the review was that it is the combination of foods in the Mediterranean diet that decreased prostate cancer incidence and mortality risk, rather than individual food components. Furthermore, in a meta-analysis summarizing the effects of adherence to a Mediterranean diet on overall cancer mortality found that the protective effects of the food components as a whole were associated with a decreased risk in cancer mortality (Schwingshackl & Hoffmann, 2015). Lastly, in a meta-analysis investigating the effects of greater adherence to a Mediterranean diet and effects on all-cause mortality, cardiovascular disease incidence and mortality, as well as cancer incidence and mortality found that a greater adherence demonstrated an 8% reduction in all-cause mortality as well as a 6% reduction in cancer incidence and mortality (Sofi, Abbate, Gensini, & Casini, 2010).

Chapter 5: Conclusion

This literature review provides a summary of the investigations into dietary patterns and cancer disease onset and progression. A Mediterranean dietary pattern is characterized by a high consumption of fruits, vegetables, complex carbohydrates, olive oil, and fish, a moderate intake of alcohol (particularly red wine), and a low intake of red meat and processed meats (Helstosky, 2009). Contrastingly, a Westernized dietary pattern is characterized by a high consumption of red meat and processed meats, dairy products, foods with saturated fat, processed foods, and simple carbohydrates, and a low to moderate intake of fruits and vegetables (Slimani et al., 2009 & Murtaugh et al., 2008). The different phytochemicals found in fruits and vegetables may contribute to antioxidant properties, which may lower overall body inflammation and inflammatory markers that have a role in tumor proliferation and development (World Cancer Research Fund, 2007). In addition, the chemical properties of omega-3 fatty acids, particularly DHA and EPA, compared to omega-6 fatty acids, found in higher quantities in red meat, may also play an anti-inflammatory role in lowering cancer risk (Liang et al., 2016). The evidence presented suggests there are beneficial roles of following a Mediterranean diet with respect to cancer diagnosis, prognosis, and management. The adoption, therefore, of a healthier dietary pattern (e.g. a Mediterranean dietary pattern) along with a healthy lifestyle should be encouraged, particularly among Americans plagued by the obesity epidemic as part of an intervention for reducing not just obesity, but also cancer risk and/or improving disease outcomes.

This review, however, has several limitations that need to be noted. First, the role of nutrition in the prevention and progression of cancer is still a relatively new field of study and there is still conflicting evidence on specific diets and nutrition's role in influencing the human

genome, i.e. nutritional genomics, to prevent cancer development and hinder its progression. Secondly, cancer itself is a very unpredictable disease with many different risk factors, including environmental and even genetic factors playing a role in its development and progression. For example, a genetic mutation that can affect the BRCA1 and BRCA2 tumor suppressor genes are known to affect the promotion of breast cancer development. Under these circumstances, even individuals who lead a healthy lifestyle and eat a healthy diet are still susceptible to breast cancer development. Another limitation of this review is the limited research performed in the United States and the Mediterranean regions on the effects of these two different dietary patterns on cancer development and outcomes.

In conclusion, the evidence from the presented literature articles supports the adoption of a Mediterranean diet and lifestyle for the improvement of cancer diagnosis, prognosis, and management.

Table 1: Literature Review on Westernized Dietary Pattern				
Research Study	**Study Type**	**Study Purpose**	**Population**	**Findings**
Mitrou et al., 2007	Prospective Cohort Study	To find the relationship between all-cause and cause-specific mortality in the National Institutes of Health-American Association of Retired Persons (NIH-AARP) Diet and Health Study.	Cohort including 380,296 participants (214,284 men and 166,012 women) with not history of chronic disease	Greater adherence to a Mediterranean dietary pattern was associated with reduction in all-cause mortality, including due to cancer and CVD in both men and women.
Murtaugh et al., 2008	Case-control Study	The examination of dietary patterns (Western, Prudent, Native Mexican, Mediterranean, and Dieter) with risk for breast cancer in Hispanic and non-Hispanic women from the Four-Corners Breast Cancer Study	Hispanic women (757 cases, 867 controls) and non-Hispanic women (1524 cases, 1598 controls)	The Western and Prudent dietary patterns were associated with a greater risk for breast cancer while the Native Mexican and Mediterranean dietary patterns were associated with lower risk of breast cancer.
Schleper et al., 2016	Survey	To assess needs of men to reduce prostate cancer risk, looking at BMI and diet as risk factors for prostate cancer	109 surveys of men's response analyzed. Majority of respondents were white, non-Hispanic men, married, retired, at least some college-level education, and lived in urban areas	The overall BMI ranged from 20.3 to 54.2, the mean was 29.5 and the median was 28.3. It was determined that "maintaining a healthy weight offers protection against aggressive prostate cancer and prostate cancer mortality."
Yang et al., 2015	Prospective Cohort Study	To evaluate the relationship between dietary patterns postdiagnosis of prostate cancer with mortality	926 men from the Physicians' Health Study Cohort	A Westernized dietary pattern was associated with higher prostate cancer-specific and all-cause mortality while the Prudent dietary pattern was related to a lower all-cause mortality after prostate cancer diagnosis

Table 2: Literature Review on Mediterranean Dietary Pattern				
Research Study	**Study Type**	**Study Purpose**	**Population**	**Findings**
Benetou et al., 2008	Prospective Cohort Study	To examine the effects of the degree of adherence to the traditional Mediterranean Diet (MD) and the incidence of cancer	25,623 individuals of the Greek segment of the EPIC study	The Mediterranean Diet (MD) was associated with lower overall cancer risk. Adherence was associated with a 12% reduction in the incidence of cancer overall. In this study, the diet as a whole decreased risk for cancer, not the individual components.
Bray et al., 2010	Meta-analysis	To describe the overall trends in prostate cancer incidence and mortality rates in 37 European countries by region	There were 24 countries included in this analysis	Countries with the highest incidence rates were Sweden, Finland, and The Netherlands; countries with the highest mortality rates were in Estonia, Latvia, Lithuania, Denmark, Norway, and Sweden; mortality rates have been decreasing for Great Britain, France, Germany, The Netherlands, Finland, and Norway.
Cottet et al., 2009	Prospective Cohort Study	To investigate the association between dietary pattern and risk of postmenopausal invasive breast cancer	2,381 postmenopausal invasive breast cancer cases among 65,374 women from the EPIC Cohort	Adherence to a diet comprising mostly of fruits, vegetables, fish, and olive/sunflower oil, along with avoidance of Western type foods, may contribute to a substantial reduction in postmenopausal breast cancer risk.
Couto et al., 2011	Review	To investigate the association between adherence to the Mediterranean dietary pattern and overall cancer risk within the EPIC study	The EPIC study (participants from 10 European countries—142,605 men and 335,873 women)	A lower overall cancer risk was found among individuals who greatly adhered to the Mediterranean diet. It was determined that 4.7% of cancers among men and 2.4% in women

				could be avoided in this population if there was a greater adherence to the Mediterranean diet.
López-Guarnido et al., 2015	Review	To examine the evidence on the effects of adherence to a Mediterranean diet on prostate cancer risk and to identify which elements of the diet are likely to protect against prostate cancer	Many research articles	There is strong evidence supporting the associations between food from the Mediterranean diet and reducing prostate cancer risk.
Mourouti et al., 2014	Case-control Study	To evaluate the association between adherence to the Mediterranean diet with breast cancer	250 newly diagnosed breast cancer female patients were age-matched to 250 female patients without breast cancer	Adherence to the Mediterranean diet was inversely associated with the likelihood of having breast cancer.
Schwingshackl & Hoffmann, 2015	Meta-analysis	To examine and summarize the available evidence on adherence to a Mediterranean diet (MD) and cancer risk	Many research articles	MD was associated with a reduced risk of overall cancer mortality and incidence of colorectal, breast, gastric, prostate, liver, and head and neck cancer. In addition, it seems that it is not just one food that contributes to this; rather, it is a result of a complex food pattern characteristic to the MD.
Slimani et al., 2009	Prospective Cohort Study	To describe the contribution of highly processed foods to total diet, nutrient intakes and patterns among 27 redefined centers in the 10 countries participating in the European Prospective Investigation into Cancer and Nutrition (EPIC)	36034 individuals (aged 35–74 years)	In southern countries (Greece, Spain, Italy and France), the overall contribution of highly processed foods to nutrient intakes was lower and consisted largely of staple or basic foods (for example, bread, pasta/rice, milk, vegetable oils)
Sofi et al.,	Meta-	To update previous meta-analysis	Prospective studies	A 2-point increase to the MD

2010	analysis	that investigated the effects of the MD on several health outcomes	concerning adherence to the MD and adverse clinical outcomes	determined a 8% reduction of death from any causes and a 6% reduction from death and/or the incidence of neoplastic diseases
Trichopoulou et al., 1995	Cohort Study	To assess dietary intake on overall survival	182 elderly subjects from 3 different villages	A one unit increase in diet score was associated with a 17% reduction in overall mortality and a four point increase was more than 50%

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